REMARKS

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Entry of the amendments is proper under 37 CFR §1.116, because the amendments place the application in condition for allowance and do not raise any new issue requiring further search and/or consideration. The amendments are necessary and were not earlier presented, because they are made in response to arguments raised in the final rejection. Entry of the amendments is thus respectfully requested.

Claims 1 and 13 have been amended to recite "wherein the metal chloride has a concentration selected from the range of a lower limit concentration of 0.2 w/v% and an upper limit concentration of 1.2 w/v%". Support for these amendments can be found on page 5, lines 17-21 of the specification. As a result, claims 2 and 4 have been cancelled.

I. Telephonic Interview

Applicant appreciates the courtesies extended to Applicant's attorney by Examiner Frazier during the telephonic interview held April 6, 2012.

During the interview, Applicant's attorney proposed to amend claims 1 and 13 to limit the concentration of the water-soluble metal chloride to 0.2-1.2 w/v%. The Examiner stated that these amendments would overcome the rejection in view of Experimental Example 1 of the specification (comparing Formulation 2 to Formulations 3-6 in Table 1), because this is a critical range that provides unexpected light-stabilizing effects on (+)-(S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino] butyric acid (hereinafter, "bepotastine") or a salt thereof over the art.

The Examiner also agreed to enter an Amendment After Final Rejection with these claim amendments. However, she will need to update her prior art search, and did not agree to allow the claims during the interview.

In addition, Applicant's attorney presented a reference stating that Carbopol is degraded by light. The Examiner agreed that a person of ordinary skill in the art would have expected Carbopol to impair the claimed invention, because Carbopol is degraded by light. As a result, Applicant's attorney maintained the position that using an ion sensitive, hydrophilic polymer, such as Carbopol, in the aqueous liquid preparation of claim 1 and the eye drop of claim 13

would materially affect the basic and novel characteristics of the claimed compositions. Applicant's attorney also pointed out that each example of Lehmussaari et al. (US 5,795,913) includes Carbopol.

In addition, Applicant's attorney stated that (1) Applicant should only be required to demonstrate unexpected results over Kita et al. (US 6,307,052), rather than a combination of Kita et al. and Lehmussaari et al., in view of MPEP 716.02(e)III; (2) adding a water-soluble metal chloride provides unexpected light-stabilization properties to a composition containing bepotastine based upon Experimental Example 4 of the specification; (3) the compounds disclosed in Lehmussaari et al. do not share any structural similarity and do not share a common structural feature that demonstrates light-stability; (4) the problems addressed by Lehmussaari et al. are completely different from the problems addressed by the present application; and (5) the position taken by the Examiner in the paragraph bridging pages 7-8 of the Office Action is clearly based upon Applicant's own specification and is therefore impermissible hindsight.

The Examiner did not specifically comment on items (1)-(5) above, but requested Applicant to include these items in a formal response to the Office Action.

Applicant has carefully considered the Examiner's comments and suggestions in preparing this Amendment.

II. Claim Rejection Under 35 U.S.C. § 103

The Examiner has rejected claims 1-10, 12 and 13 under 35 U.S.C. § 103(a) as being unpatentable over Kita et al. (US 6,307,052) in view of Lehmussaari et al. (US 5,795,913). As applied to the amended claims, Applicant respectfully traverses the rejection.

The Concentration of the Metal Chloride

Kita et al. teach a medical composition comprising bepotastine, but the reference does not specifically teach how the composition is formulated and does not specifically teach a water-soluble metal chloride in a light-stabilizing effective amount.

As discussed above, claims 1 and 13 have been amended to recite that the concentration of the water-soluble metal chloride is 0.2-1.2 w/v%, and, as agreed during the interview, this is a critical range that provides unexpected light-stabilizing effects over the art. Moreover, claim 10 has an even narrower metal chloride concentration of 0.2-0.8 w/v%. Thus, as demonstrated by Experimental Example 1 of the specification, Formulation 2, comprising 0.1 w/v% of a metal

chloride (sodium chloride) fails to light-stabilize bepotastine besilate, because after light irradiation it was slightly dark green-pale yellow and produced a precipitate. On the other hand, Formulations 3-6, comprising 0.2 to 1.18 w/v% of a metal chloride (i.e., sodium chloride, potassium chloride or calcium chloride), provide an unexpected light-stabilizing effect, because after light irradiation the formulations were pale yellow and clear and no precipitate was formed.

Moreover, sodium chloride, potassium chloride and calcium chloride, as recited in claim 3, are generally added to eye drops as tonicity agents. However, as demonstrated in Experimental Example 4 of the specification, glycerin, glucose and mannitol, which are generally used tonicity agents other than metal chlorides, fail to demonstrate a light-stabilizing effect. Therefore, the effect of light-stabilizing an aqueous bepotastine solution with a metal chloride is completely unexpected.

Accordingly, as agreed during the interview, the concentration of 0.2-1.2 w/v% is a critical range that provides unexpected results in terms of light-stabilization over Kita et al. (see MPEP 2144.05.III and 716.02(e)III).

Carbopol

In addition, claims 1 and 13 recite the transitional phrase "consisting essentially of", which limits the scope of a claim to the specified materials or steps and those that do not materially affect the basic and novel characteristic(s) of the claimed invention (see MPEP 2111.03).

As agreed during the interview, the composition of Lehmussaari et al. requires the inclusion of an ion sensitive, hydrophilic polymer having viscosity, such as Carbopol, to control the formation of the polymer film on the cornea of the eye, and each of the reference's examples contain Carbopol (please see col. 2, line 57 to col. 3, line 6, and the Examples). However, a person of ordinary skill in the art would recognize that Carbopol is degraded by light, as evidenced by the enclosed Chemical Abstract reference, which states "CARBOXYVINYL POLYMERS of the type Carbopol 940…and 941 were degraded by light, type 941 presenting the highest DEGRADATION" (emphasis in original).

Therefore, using an ion sensitive, hydrophilic polymer, such as Carbopol, in the aqueous liquid preparation of claim 1 and the eye drop of claim 13 would materially affect the basic and novel characteristics of the claimed compositions. As a result, an ion sensitive, hydrophilic polymer is excluded from the claimed compositions, and a person of ordinary skill in the art

could not have arrived at the presently claimed invention from the combination of Kita et al. and Lehmussaari et al. with any reasonable expectation of success.

Difference of Problems

Furthermore, the objective of Lehmussaari et al. is "to provide an ophthalmic composition with a sufficiently high concentration of polymer to control the formation of the polymer film on the cornea of the eye, but which composition is still fluid enough for ocular topical application" (see col. 1, line 65 to col. 2, line 3).

On the other hand, the objective of the claimed invention is to light-stabilize bepotastine or a salt thereof in an aqueous solution. A person of ordinary skill in the art would recognize that the light-stabilization of a drug and the viscosity control of a composition for local administration are completely different problems. Accordingly, there would have been no reason or rationale to combine Kita et al. with Lehmussaari et al. to obtain light-stabilization of bepotastine.

Difference in Compounds

In addition, Lehmussaari et al. describe, as an active ingredient containing a basic group, about 30 compounds having completely different chemical structures (see col. 3, line 66 to col. 4, line 27). In general, chemical properties, such as light-stability, vary according to the chemical structure. There is no reasonable basis for these compounds, having no structural similarity, to have uniform light-stability from the teachings of the reference. Thus, a person of ordinary skill in the art would not have had any reason to use the compounds disclosed in Lehmussaari et al. to light-stabilize bepotastine, as in the presently claimed invention.

Hindsight

In the paragraph bridging pages 7-8 of the Office Action, the Examiner has asserted that one skilled in the art would have been motivated to manipulate the amount of salt disclosed in Lehmussaari et al. by routine experimentation in order to optimize the viscosity reducing effects, and such amount would necessarily be a light-stabilizing effective amount, as evidenced by Applicant's own specification.

However, as discussed above, Lehmussaari et al. teach to use an agent that is degraded by light in each example (Carbopol) and teach a wide-range of compounds with no structural similarity and no effect on light-stability. Accordingly, the Examiner's position is based solely on Applicant's own specification, which teaches that a water-soluble metal chloride has a light-

stabilizing effect on bepotastine. Therefore, the Examiner's position is based upon impermissible hindsight reasoning.

Conclusion of Non-Obviousness

Accordingly, in view of the foregoing amendments and remarks, claims 1, 10 and 13 would not have been obvious over Kita et al. in view of Lehmussaari et al.

Claims 3, 5-9 and 12 depend directly or indirectly from claim 1, and thus also would not have been obvious over the references.

Therefore, reconsideration and withdrawal of the rejection are respectfully requested.

III. Conclusion

For these reasons, Applicant takes the position that the presently claimed invention is clearly patentable over the applied references.

Therefore, in view of the foregoing amendments and remarks, it is submitted that the rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

Respectfully submitted,

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